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A Stroke in the Young with Surprising Recovery

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ABSTRACT

Introduction: The differential diagnosis of stroke in a comparatively young adult should always include cardiovascular aetiologies as well as central nervous system infection.

Case Presentation: A 56-year-old man, with no significant medical history, presented with headache, nausea and vomiting, and right hemiparesis. Routine stroke investigation was initiated, while CNS infection was also sought. Diagnoses of HIV infection, neurosyphilis, HCV and HBV were established. Targeted therapy resulted in prompt clinical improvement.

Conclusion: This case highlights the importance of considering CNS infection as a cause of neurological deficits in parallel with other investigations in cases of stroke in a comparatively young adult.

LEARNING POINTS

- The differential diagnosis should be wide for all patients presenting with stroke.
- Neurosyphilis should be included in the differential diagnosis of stroke in the young and middle-aged.
- Newly diagnosed HIV patients should be screened for other, sexually transmitted coinfection.

KEYWORDS

Stroke in the young, neurosyphilis, AIDS, HIV, syphilis, HCV

CASE DESCRIPTION

A 56-year-old man with no significant medical history presented to hospital with right hemiparesis which had developed gradually over 2–3 days. He had recently immigrated to Israel from Russia, spoke very little Hebrew and worked as a janitor. After initial workup, as the symptoms had lasted for over 24 hours, the patient was admitted to the internal medicine department with suspected stroke since there were no vacant beds in the neurology department. Vital signs were normal at admission. The patient's general appearance was unkempt; substance abuse, promiscuous sexual activity and exotic travel were denied. His physical examination revealed normal heart sounds without murmurs and bilateral vesicular breathing sounds on both lungs. The abdomen was soft and non-tender without any evidence of organomegaly. There was no evidence of pedal oedema. Skin examination revealed tinea unguium on all digits of the left hand. The patient had prominent facial seborrheic dermatitis. Neurological examination revealed mild seventh cranial nerve palsy on the left with right hemiparesis (strength of 3/5 in the right lower and upper limbs). Further investigation revealed abnormal liver function tests with elevated AST (139 IU/l), ALT (85 IU/l) and GGT (282 IU/l). CT of the brain (without contrast material) was normal. An electrocardiogram showed normal sinus rhythm. A posterior-anterior chest x-ray was normal.

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Routine workup and management of stroke in a middle-aged adult were initiated upon admission. The patient's comparatively young age, low socioeconomic status and the fact that he was an immigrant, along with the dermatological findings, suggested CNS infection should be ruled out. Serological testing using the HIV combo test and immunoblot assay, HBV-hepatitis B core antigen (S/CO) and hepatitis B anti-surface (HbsAg) antibody (mIU/ml) including hepatitis Be antigen, HCV-hepatitis C antibody (S/CO) and syphilis-RPR, were all positive (*Table 1*). The CD4 count was 230 cells/mm^3. The opening pressure of a lumbar puncture was 160 cm H_2O. The CSF cell count was 66 cells/mm^3 (PMN cells and mononuclear cells), the protein level was elevated (64 mg/dl), and glucose and lactate levels were within the normal range. CSF real-time PCR was positive for JC virus but negative for cryptococcal antigen, *Toxoplasma gondii*, *Toxoplasma gondii* IGM and syphilis VDRL. Culture for mycobacteria was negative.

The initial CT scan of the brain mentioned above was normal. However, MRI of the brain showed subacute stroke in the medulla together with general subcortical microangiopathic changes. Several characteristic findings associated with neurosyphilis were also seen. These included general atrophy, mesial temporal atrophy (*Fig. 1*) as well as an infarct in the midline medulla and left pyramid (*Figs. 2 and 3*). Further CT angiographic studies ruled out large-vessel vasculitis and other significant vascular anomalies. Trans-thoracic echocardiography showed no evidence of endocarditis.

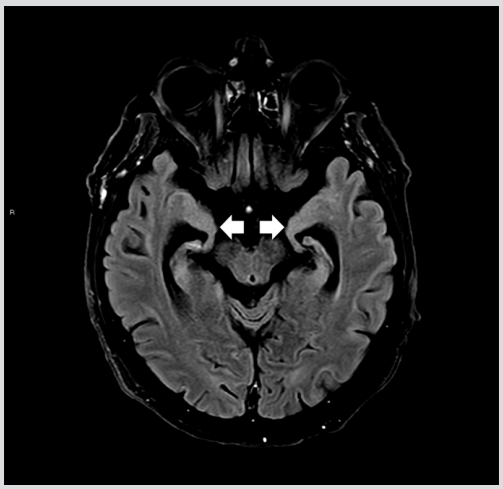

Figure 1. T2 FLAIR weighted image showing symmetrical atrophy (white arrowheads) of the mesial temporal lobes

Figure 2. Diffusion weighted MRI image showing an infarct (white arrowhead) in the acute phase midline medulla and left pyramid

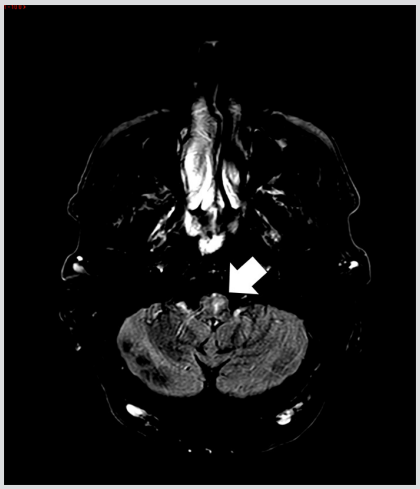

Figure 3. T2 FLAIR MRI image showing an acute infarct (white arrowhead) in the midline medulla and left pyramid

	Patient	Normal Range
Cerebrospinal fluid		
Glucose (mg/dl)	50	50-80
Lactate (mg/dl)	18.4	10-25
Protein (mg/dl)	64.8	22-38
WBC (cells/mm^3)	66	0-5
VDRL antigen	Negative	-
Cryptococcal antigen	Negative	-
Toxoplasma PCR and toxoplasma IGM	Negative	
JC virus RT-PCR	Positive	
TB culture	Negative	

	Patient	Normal Range
Hepatitis serology		
Hepatitis B core total (S/CO)	6.8	
Anti-HBsAg (mIU/ml)	205	
Hepatitis Be antibody (S/CO)	0.02	
Hepatitis C antibody (S/CO)	15.08	
HIV immunoblot	Positive	
Syphilis RPR	1:32	
Syphilis CMIA (S/CO)	21.88	

Table 1. Laboratory investigation results

HBsAg, hepatitis B surface antigen; PCR, polymerase chain reaction; RT-PCR, real-time polymerase chain reaction; TB, tuberculosis.

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After a working diagnosis of neurosyphilis was established, the patient was treated with intra-muscular benzathine penicillin G (for syphilis) and intravenous penicillin G sodium (for neurosyphilis) for 10 days. There was no Jarisch-Herxheimer reaction. Anti-retroviral treatment with a combination of dolutegravir, tenofovir and emtricitabine for HIV was also initiated. The patient received daily physiotherapy. Neurological improvement was noted and after 30 days of hospitalization, the patient was discharged and referred for continued rehabilitation.

DISCUSSION

The aetiology of stroke in comparatively young adults is diverse and varies according to age and geographical region. Non-cerebrovascular stroke accounts for 20–30% of cases. A wide variety of different and uncommon causes of stroke in young adults is described in the literature and includes non-atherosclerotic angiopathies, antiphospholipid syndrome, sickle cell disease, inherited syndromes (e.g., mitochondrial encephalopathy, lactic acidosis and stroke-like episodes (MELAS) and Fabry disease), and inflammatory and infectious agents (including HIV, neurosyphilis and Varicella zoster virus), along with several types of vasculitides[1].

Syphilis is a sexually transmitted, chronic systemic infection caused by *Treponema pallidum*. Prevalence in developing countries can reach 25% among blood donors. Israel receives immigrants from all over the world, particularly from the former Soviet Union and Africa. The WHO European Health database shows that Eastern European and African countries have a high incidence of syphilis[2].

In newly diagnosed HIV patients who present with focal neurological findings, the differential diagnosis includes toxoplasmosis, progressive multifocal leukoencephalopathy due to JC virus, CNS lymphoma and stroke[3]. Neurosyphilis can present at any stage of the disease. The clinical categories of symptomatic neurosyphilis include meningeal, meningovascular and parenchymatous syphilis. Meningovascular disease, through the mechanism of small, medium and large vessel arteritis, can manifest as an infarct indistinguishable from cerebrovascular stroke[4]. The diagnosis of neurosyphilis in HIV patients can be difficult for several reasons: (a) CSF serology for VDRL may only be positive in approximately one third of cases; (b) HIV infection itself can cause CSF pleocytosis and an increased protein level; and (c) HIV-associated vasculopathy can contribute to inflammation of the cerebral blood vessels through different mechanisms such as vasculitis, accelerated atherosclerosis and aneurysm formation[5, 6]. Brain MRI findings may demonstrate characteristic but non-specific findings of neurosyphilis, including general atrophy and mesial temporal atrophy[7], as well as infarct in the midline medulla and left pyramid (as described in our patient).

This case highlights the importance of considering CNS infections as a cause of neurological deficits in conjunction with other investigations in comparatively young patients presenting with stroke. Thrombolysis was not administered to our patient due to the delay between clinical presentation and treatment initiation. The gradual onset of symptoms should always suggest infection as the cause of a stroke in progress. In their retrospective review of 53 patients with syphilitic vasculitis affecting the central nervous system, Ahbeddou et al. described a prodromal phase preceding signs of stroke[8]. We do not know the effect thrombolysis would have had in our patient, since there is no relevant literature. Our case also highlights the complexity of the management of newly diagnosed HIV patients with syphilis coinfection. Even with a non-reactive CSF VDRL test, the combination of newly diagnosed HIV infection together with positive syphilis serum serology, new onset of focal neurological findings and pathological CNS findings is sufficient to prompt treatment initiation.

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